

1           1. A DNA construct that alters expression of an  
2 endogenous G-CSF gene in a mammalian cell upon integration  
3 into the genome of the cell via homologous recombination,  
4 the construct comprising: (i) a targeting sequence  
5 containing at least 20 contiguous nucleotides from  
6 SEQ ID NO:5 and (ii) a transcriptional regulatory sequence.

1           2. The DNA construct of claim 1, wherein the  
2 construct further comprises an exon and a splice-donor site.

1           3. The DNA construct of claim 2, wherein the  
2 construct further comprises, downstream from the splice-  
3 donor site, an intron and a splice-acceptor site.

1           4. The DNA construct of claim 1, wherein the  
2 construct further comprises a selectable marker gene.

1           5. The DNA construct of claim 1, wherein the  
2 targeting sequence contains at least 50 contiguous  
3 nucleotides from SEQ ID NO:5.

1           6. An isolated nucleic acid comprising at least 20  
2 contiguous nucleotides of SEQ ID NO:5 or its complement,  
3 wherein the isolated nucleic acid does not encode full-  
4 length G-CSF.

1           7. The isolated nucleic acid of claim 6, wherein  
2 the isolated nucleic acid comprises at least 50 contiguous  
3 nucleotides of SEQ ID NO:5 or its complement.

1           8. The isolated nucleic acid of claim 6, wherein  
2 the isolated nucleic acid comprises at least 100 contiguous  
3 nucleotides of SEQ ID NO:5 or its complement.

1           9. The isolated nucleic acid of claim 6, wherein  
2 the isolated nucleic acid comprises at least 200 contiguous  
3 nucleotides of SEQ ID NO:5 or its complement.

1           10. The isolated nucleic acid of claim 6, wherein  
2 the isolated nucleic acid comprises at least 500 contiguous  
3 nucleotides of SEQ ID NO:5 or its complement.

1           11. The isolated DNA of claim 6, wherein the  
2 isolated nucleic acid comprises nucleotides 1470 to 4723 of  
3 SEQ ID NO:5, or its complement.

1           12. The isolated DNA of claim 6, wherein the  
2 isolated nucleic acid comprises SEQ ID NO:5 or its  
3 complement.

1           13. An isolated nucleic acid comprising a strand  
2 that comprises a nucleotide sequence that (i) is at least  
3 100 nucleotides in length and (ii) hybridizes under highly  
4 stringent conditions with SEQ ID NO:5 or the complement  
5 thereof.

1           14. The isolated nucleic acid of claim 13, wherein  
2 the nucleotide sequence is at least 200 nucleotides in  
3 length.

1           15. The isolated nucleic acid of claim 13, wherein  
2 the nucleotide sequence is at least 400 nucleotides in  
3 length.

1           16. The isolated nucleic acid of claim 13, wherein  
2 the nucleotide sequence is at least 1,000 nucleotides in  
3 length.

1           17. An isolated nucleic acid comprising a strand  
2 that comprises a nucleotide sequence that (i) is at least  
3 100 nucleotides in length and (ii) shares at least 80%  
4 sequence identity with a fragment of SEQ ID NO:5 having the  
5 same length as the nucleotide sequence.

1           18. The isolated nucleic acid of claim 17, wherein  
2 the nucleotide sequence is at least 200 nucleotides in  
3 length.

1           19. The isolated nucleic acid of claim 18, wherein  
2 the nucleotide sequence is at least 400 nucleotides in  
3 length.

1           20. The isolated nucleic acid of claim 18, wherein  
2 the nucleotide sequence is at least 1,000 nucleotides in  
3 length.

1           21. A homologously recombinant cell stably  
2 transfected with the DNA construct of claim 1, the DNA  
3 construct having undergone homologous recombination with  
4 genomic DNA upstream of the ATG initiation codon of an  
5 endogenous G-CSF coding sequence.

1           22. A homologously recombinant cell stably  
2 transfected with the DNA construct of claim 2, the DNA  
3 construct having undergone homologous recombination with  
4 genomic DNA upstream of the ATG initiation codon of an  
5 endogenous G-CSF coding sequence.

1           23. A homologously recombinant cell stably  
2 transfected with the DNA construct of claim 3, the DNA  
3 construct having undergone homologous recombination with  
4 genomic DNA upstream of the ATG initiation codon of an  
5 endogenous G-CSF coding sequence.

1           24. A homologously recombinant cell stably  
2 transfected with the DNA construct of claim 4, the DNA  
3 construct having undergone homologous recombination with  
4 genomic DNA upstream of the ATG initiation codon of an  
5 endogenous G-CSF coding sequence.

1           25. A method of altering expression of an  
2 endogenous G-CSF gene in a mammalian cell, the method  
3 comprising

4                 introducing the DNA construct of claim 1 into the  
5 cell;

6                 maintaining the cell under conditions which permit  
7 homologous recombination to occur between the construct and  
8 a genomic target site homologous to the targeting sequence,  
9 to produce a homologously recombinant cell; and

10                maintaining the homologously recombinant cell under  
11 conditions which permit expression of the G-CSF coding  
12 sequence under the control of the transcriptional regulatory  
13 sequence.

1           26. A method of altering expression of an  
2 endogenous G-CSF gene in a mammalian cell, the method  
3 comprising  
4           introducing the DNA construct of claim 4 into the  
5 cell;  
6           maintaining the cell under conditions which permit  
7 homologous recombination to occur between the construct and  
8 a genomic target site homologous to the targeting sequence,  
9 to produce a homologously recombinant cell; and  
10          maintaining the homologously recombinant cell under  
11 conditions which permit expression of the G-CSF coding  
12 sequence under the control of the transcriptional regulatory  
13 sequence.

1           27. A method of delivering G-CSF to an animal,  
2 comprising  
3           providing the cell of claim 21, and  
4           implanting the cell in the animal, wherein the cell  
5 secretes G-CSF.

1           28. A method of delivering G-CSF to an animal,  
2 comprising  
3           providing the cell of claim 22, and  
4           implanting the cell in the animal, wherein the cell  
5 secretes G-CSF.

1           29. A method of delivering G-CSF to an animal,  
2 comprising  
3           providing the cell of claim 23, and  
4           implanting the cell in the animal, wherein the cell  
5 secretes G-CSF.

1           30. A method of delivering G-CSF to an animal,  
2 comprising  
3           providing the cell of claim 24, and  
4           implanting the cell in the animal, wherein the cell  
5 secretes G-CSF.

1           31. A method of producing G-CSF, comprising  
2           providing the cell of claim 21, and  
3           culturing the cell *in vitro* under conditions which  
4 permit the cell to express and secrete G-CSF.

1           32. A method of producing G-CSF, comprising  
2           providing the cell of claim 22, and  
3           culturing the cell *in vitro* under conditions which  
4 permit the cell to express and secrete G-CSF.

1           33. A method of producing G-CSF, comprising  
2           providing the cell of claim 23, and  
3           culturing the cell *in vitro* under conditions which  
4 permit the cell to express and secrete G-CSF.

1           34. A method of producing G-CSF, comprising  
2           providing the cell of claim 24, and  
3           culturing the cell *in vitro* under conditions which  
4 permit the cell to express and secrete G-CSF.